

Amendment to the Claims

Claim 1 (withdrawn): A method for producing a heritable integration of a transgene within a genome of a somatic or germ line cell of an invertebrate organism, the method comprising:

providing a first DNA cassette within said genome, wherein said first cassette comprises a first flanking transposon half side, a second flanking transposon half side, and an internal transposon half side, wherein said internal transposon half side and said first flanking transposon half side form a pair of excisable transposon half-sides, and wherein said first cassette further comprises said transgene in-between the internal transposon half side and said second flanking transposon half side; and

mobilizing said excisable transposon half-sides.

Claim 2 (withdrawn): The method of claim 1, wherein said internal transposon half side and said second flanking transposon half side are TransposonL half sides, and wherein said first flanking transposon half side is a TransposonR half side.

Claim 3 (withdrawn): The method of claim 1, wherein said internal transposon half side and said second flanking transposon half side are TransposonR half sides, and wherein said first flanking transposon half side is a TransposonL half side.

Claim 4 (withdrawn): The method of claim 1, wherein said excisable transposon half-sides and corresponding transposase enzyme are from a transposable element, wherein said transposable element has terminal inverted sequences, and wherein said transposable element transposes via a DNA-mediated process.

Claim 5 (withdrawn): The method of claim 1, wherein said first DNA cassette further comprises a first selectable marker gene located between said internal transposon half side and said first flanking transposon half side, and a second selectable marker gene located between said internal transposon half side and said second flanking transposon half side, and wherein said first and second selectable marker genes are phenotypically distinguishable.

Claim 6 (withdrawn): The method of claim 5, wherein said first and second marker genes are, in either order, any combination of marker genes producing distinguishable fluorescent or other visible dominant phenotypes.

Claim 7 (withdrawn): The method of claim 5 wherein said first and second marker genes are, in either order, a combination of the transformation marker genes PUbDsRed1 and 3xP3-ECFP.

Claim 8 (withdrawn): The method of claim 1, wherein said internal transposon half side is provided in reverse orientation, wherein said excisable transposon is formed by inversion of said internal transposon half side relative to said first flanking transposon half side, wherein said internal transposon half side further comprises flanking recombinase sites, and wherein said inversion is catalyzed by a site-specific recombinase.

Claim 9 (withdrawn): The method of claim 8, wherein said recombinase sites are FRT sites in opposite or reverse orientation.

Claim 10 (withdrawn): The method of claim 1, wherein said excisable transposon is mobilized by a source of transposase corresponding to said excisable transposon to render the remaining genomic DNA immobilizable.

Claim 11 (currently amended): A method for targeting a heritable integration of a transgene within a genome of a somatic or germ line cell of an invertebrate organism, said method comprising:

integrating a first DNA cassette within said genome by transposase-mediated integration of flanking transposon half sides, wherein said first cassette comprises a wild-type/non-mutated or a mutated target site of a site-specific recombinase at one end and a mutated target site of said site-specific recombinase at an other end, wherein said recombinase target sites are heterospecific, and wherein said target sites flank marker gene DNA and flank additional DNA sequence, and selecting an integration site within said genome with said first DNA cassette integrated; and

exchanging said first DNA cassette for a second DNA cassette by a site-specific recombinase enzyme that catalyzes a DNA recombination reaction via homospecific recombinase target sites, wherein the second DNA cassette comprises heterospecific site-specific recombinase target sites

that are homospecific and in the same orientation with the wild-type/non-mutated or a mutated target site of a site-specific recombinase of the first cassette at one end and a mutated target site of said site-specific recombinase homospecific to said recombinase target site of the first cassette at an other end, with said target sites of the second cassette flanking an internal transposon half side, wherein the internal half side is excisable with a flanking transposon half side of the first DNA cassette, and internal transposon half side, wherein said target sites flank additional DNA sequence.

Claim12 (previously presented): The method of claim 11, wherein said site-specific recombinase is FLP recombinase, and wherein said recombinase target sites are FRT sites or mutated derivatives of said FRT sites.

Claim 13 (previously presented): The method of claim 11, wherein said site-specific recombinase is Cre recombinase, and wherein said recombinase target sites are loxP sites or mutated derivatives of said loxP sites.

Claim 14 (previously presented): The method of claim 11, wherein one of the target sites of said first cassette is a site-specific recombinase target site placed in-between a marker gene coding region and a promoter DNA that regulates its expression.

Claim 15 (previously presented): The method of claim 11, wherein said first cassette comprises a homing sequence to enhance pairing to said site-specific recombinase target sites in said second cassette.

Claim 16 (previously presented): The method of claim 11, wherein said homing sequence comprises a DNA sequence hybridizing to a *Drosophila* linotte locus.

Claim 17 (previously presented): The method of claim 11, wherein the additional DNA sequence of the second cassette comprises the target nucleotide sequence of said transgene.

Claim 18 (previously presented): The method of claim 11, wherein said second cassette comprises a marker gene coding region lacking a promoter for regulating its expression, and wherein, following the exchange of said first DNA cassette to said second cassette, said marker gene is placed under the control of said promoter derived from said first cassette.

Claim 19 (previously presented): The method of claim 15, wherein said second cassette comprises the same homing sequence as said first cassette within said recombinase target sites.

Claim 20 (previously presented): The method of claim 11, wherein said transposon half side in-between said recombinase target sites with phenotypically distinguishable marker genes on either side, wherein one of said marker genes lacks a promoter.

Claim 21 (currently amended): The method of claim 11, wherein the first cassette further comprises an operable promoter, wherein site-specific recombinase mediated insertion occurs between a coding region of said second cassette and ~~an~~ a said operable promoter of a selectable

marker gene of said first cassette.

Claim 22 (currently amended): The method of claim 20, ~~wherein said internal transposon half side is excisable with a flanking transposon half side, and~~ wherein said excisable transposon is mobilized by a source of transposase corresponding to said excisable transposon to render the remaining genomic DNA immobilizable.

Claim 23 (withdrawn): An invertebrate organism comprising the heritable transgene produced according to claim 1.

Claim 24 (previously presented): An invertebrate organism comprising the heritable transgene produced according to claim 11.

Claim 25 (withdrawn): A method for producing a heritable integration of a transgene within a genome of a somatic or germ line cell of an organism, the method comprising:

providing a first DNA cassette within said genome, wherein said first cassette comprises a first flanking transposon half side, a second flanking transposon half side, and an internal transposon half side, wherein said internal transposon half side and said first flanking transposon half side form a pair of excisable transposon half-sides, and wherein said first cassette further comprises said transgene in-between the internal transposon half side and said second flanking transposon half side; and

mobilizing said excisable transposon half-sides.

Claim 26 (withdrawn): The method of claim 25, wherein said internal transposon half side and said second flanking transposon half side are TransposonL half sides, and wherein said first flanking transposon half side is a TransposonR half side.

Claim 27 (withdrawn): The method of claim 25, wherein said internal transposon half side and said second flanking transposon half side are TransposonR half sides, and wherein said first flanking transposon half side is a TransposonL half side.

Claim 28 (withdrawn): The method of claim 25, wherein said excisable transposon half-sides and corresponding transposase enzyme are from a transposable element, wherein said transposable element has terminal inverted sequences, and wherein said transposable element transposes via a DNA-mediated process.

Claim 29 (withdrawn): The method of claim 25, wherein said first DNA cassette further comprises a first selectable marker gene located between said internal transposon half side and said first flanking transposon half side, and a second selectable marker gene located between said internal transposon half side and said second flanking transposon half side, and wherein said first and second selectable marker genes are phenotypically distinguishable.

Claim 30 (withdrawn): The method of claim 29, wherein said first and second marker genes are, in either order, any combination of marker genes producing distinguishable fluorescent or other visible dominant phenotypes.

Claim 31 (withdrawn): The method of claim 29, wherein said first and second marker genes are, in either order, a combination of the transformation marker genes PUBDsRed1 and 3xP3-ECFP.

Claim 32 (withdrawn): The method of claim 25, wherein said internal transposon half side is provided in reverse orientation, wherein said excisable transposon is formed by inversion of said internal transposon half side relative to said first flanking transposon half side, wherein said internal transposon half side further comprises flanking recombinase sites, and wherein said inversion is catalyzed by a site-specific recombinase.

Claim 33 (withdrawn): The method of claim 32, wherein said recombinase sites are FRT sites in opposite or reverse orientation.

Claim 34 (withdrawn): The method of claim 25, wherein said excisable transposon is mobilized by a source of transposase corresponding to said excisable transposon to render the remaining genomic DNA immobilizable.

Claim 35 (currently amended): A method for targeting a heritable integration of a transgene within a genome of a somatic or germ line cell of an organism, said method comprising:



integrating a first DNA cassette within said genome by transposase-mediated integration of flanking transposon half sides, wherein said first cassette comprises a wild-type/non-mutated or a mutated target site of a site-specific recombinase at one end and a mutated target site of said site-specific recombinase at an other end, wherein said recombinase target sites are heterospecific, and wherein said target sites flank marker gene DNA and flank additional DNA sequence, and

selecting an integration site within said genome with said first DNA cassette integrated; and

exchanging said first DNA cassette for a second DNA cassette by a site-specific recombinase enzyme that catalyzes a DNA recombination reaction via [a] homospecific recombinase target sites, wherein the second DNA cassette comprises heterospecific site-specific recombinase target sites that are homospecific and in the same orientation with the wild-type/non-mutated or a mutated target site of a site-specific recombinase of the first cassette at one end and a mutated target site of said site-specific recombinase homospecific to said recombinase target site of the first cassette at another end with said target sites flanking an internal transposon half side, wherein the internal half side is excisable with a flanking transposon half side of the first DNA cassette, and internal transposon half side, wherein said target sites flank additional DNA sequence.

Claim 36 (previously presented): The method of claim 35, wherein said site-specific recombinase is FLP recombinase, and wherein said recombinase target sites are FRT sites or mutated derivatives of said FRT sites.

Claim 37 (previously presented): The method of claim 35, wherein said site-specific recombinase is Cre recombinase, and wherein said recombinase target sites are loxP sites or mutated derivatives of said loxP sites.

Claim 38 (previously presented): The method of claim 35, wherein one of the target sites of said first cassette is a site-specific recombinase target site placed in-between a marker gene coding region and a promoter DNA that regulates its expression.

Claim 39 (previously presented): The method of claim 35, wherein said first cassette comprises a homing sequence to enhance pairing to said site-specific recombinase target sites in said second cassette.

Claim 40 (previously presented): The method of claim 35, wherein said homing sequence comprises a DNA sequence hybridizing to a *Drosophila* linotte locus.

Claim 41 (previously presented): The method of claim 35, wherein the additional DNA sequence of the second cassette comprises the target nucleotide sequence of said transgene.

Claim 42 (previously presented): The method of claim 35, wherein said second cassette comprises a marker gene coding region lacking a promoter for regulating its expression, and wherein, following the exchange of said first DNA cassette to said second cassette, said marker gene is placed under the control of said promoter derived from said first cassette.

Claim 43 (previously presented): The method of claim 39, wherein said second cassette comprises the same homing sequence as said first cassette within said recombinase target sites.

Claim 44 (previously presented): The method of claim 35, wherein said transposon half side in-between said recombinase target sites with phenotypically distinguishable marker genes on either side, wherein one of said marker genes lacks a promoter.

Claim 45 (currently amended): The method of claim 35, wherein the first cassette further comprises an operable promoter, wherein site-specific recombinase mediated insertion occurs between a coding region of said second cassette and ~~an~~ said operable promoter of a selectable marker gene of said first cassette.

Claim 46 (previously presented): The method of claim 44, wherein said internal transposon half side is excisable with a flanking transposon half side, and wherein said excisable transposon is mobilized by a source of transposase corresponding to said excisable transposon to render the remaining genomic DNA immobilizable.

Claim 47 (withdrawn): An organism comprising the heritable transgene produced according to claim 25.

Claim 48 (previously presented): An organism comprising the heritable transgene produced according to claim 35.